GlaxoWellcome

Maury M. Tepper, III
Trademark Attorney
Global Intellectual Property

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Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

RE: FDA DRAFT GUIDANCE FOR INDUSTRY:
PLACING THE THERAPEUTIC EQUIVALENCE CODE ON
PRESCRIPTION DRUG LABELS AND LABELING

Dear Sirs:

Glaxo Wellcome Inc. hereby submits these comments to the FDA Draft Guidance identified above, made available on January 28, 1999. Glaxo Wellcome is a research-based pharmaceutical company, devoted to discovering medicines that improve the lives and health of patients.

Introduction

The matter at issue in these comments is whether the immediate container and carton labeling of a generic drug are an appropriate location for therapeutic equivalency statements. Such statements have since 1980 appeared in the *Orange Book*. The draft Guidance proposes allowing or mandating the manufacturer of a generic drug to use the trademark of a brand-name competitor as part of a therapeutic equivalency statement on the label of a generic drug. The recommended statement is in the form, to borrow from the draft Guidance, "This product is AB to CHICOSE®. CHICOSE® is a registered trademark of Marx Brothers, Inc." We believe that the principal effect of such use of a trademark would be to create confusion and possible mistaken product substitutions, with attendant risks to patients. This kind of confusion would be wholly inconsistent with well-settled tenets of trademark law.

The Potential for Harmful Mistakes and Confusion

The placement of a well-established, instantly identifiable trademark on the label of a competitor's product as part of an equivalency statement may cause pharmacists and other health professionals to easily and falsely attribute the product's origin to the brand-name manufacturer. Many generic drugs carry no brand names on their labels. If the only brand name on a drug label is that of the innovator company, as would be the case in accordance with the proposed equivalency statement set forth in the Guidance, the likelihood of confusion and false attribution

Glaxo Wellcome Inc.
Five Moore Drive
PO Box 13398
Research Triangle Park
North Carolina 27709-3398
Telephone
919 483 2519
Fax
919 483 7988

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98D-1266

of origin are significantly greater. The proposed labeling scheme is not sufficient to dispel this confusion in that the wording is not sufficient to clearly differentiate the trademark owner from the generic drug manufacturer, and there are insufficient controls over the placement and appearance of the permitted statements.

The likely confusion is most worrisome in that it could result in pharmacists and consumers actually mistaking the generic product for the branded innovator product, under circumstances in which the inadvertent substitution could have grave consequences. For instance, if a patient is known to have an allergy or adverse reaction to an excipient in a generic product and the prescriber has therefore been careful to specify and insist on the brand name product, the use on the label of a generic product of an equivalency statement linked to the brand name of the innovator product, as proposed by the Guidance, presents an unwarranted danger that the patient could nonetheless mistakenly receive the generic product. Given the availability of complete therapeutic equivalence information in the *Orange Book*, as discussed more fully below, this risk need not be tolerated.

Although risks to patient welfare, as described above, are our principal concern, please understand that the confusion apt to be engendered by this proposed labeling practice would also be untenable under established principles of trademark law and could subject generic companies placing such statements on their product labeling to liability for trademark infringement. The Lanham Act prohibits any use of a mark that would create a likelihood of confusion as to the source or origin of a product, or as to the existence of an affiliation, sponsorship or other connection between the owner of the trademark and another party. (15 U.S.C. §§ 1114, 1125). The primary objective of trademark law is to promote the public's ability to associate a product identified by a trademark as being the product of the mark's owner and to protect the consuming public from being misled or deceived by the use of confusingly similar marks or by misleading uses of a trademark. In the context of pharmaceutical products that may not be interchangeable for patients with distinctive medical histories and needs, the public interest served is broader than economic protection: it is promotion of public health as well. Although brief equivalency statements of the kind proposed by the Guidance may be factually accurate, they would be misleading, and for that reason constitute trademark infringement and unfair competition in violation of the federal trademark laws.

There is another respect in which the labeling statements suggested in the Guidance could result in inappropriate product selection. Unlike the complete therapeutic equivalence information published in the *Orange Book* (which is updated monthly and which is available instantaneously over the internet), brief therapeutic equivalence declarations on the labels of products already in commercial distribution are not readily subject to revision. Although such declarations may become dated, and potentially harmful to patients in their inaccuracy, there would be no satisfactory mechanism for correcting them when the need arises. Although the Guidance alleges that "Pharmacists and other health professionals who practice drug product selection for patients will become more knowledgeable about which product may be safely

substituted for another," this clearly cannot be the case if the equivalency information they consult is outdated or otherwise incorrect.

In a more general sense, the approach proposed in the Guidance raises the prospect of unnecessary misunderstanding and confusion on the part of pharmacists and consumers. The therapeutic rating system that FDA employs (and which is summarized on page 4 of the Guidance) is very complex. It is understood imperfectly by many pharmacists and not at all by most patients. Persons encountering a brief therapeutic equivalency statement on the label of a generic product would therefore be unable to comprehend it or even minimally grasp its significance. No patient could be expected to readily appreciate the important differences between a statement that a product is "AB" and a statement that a product is "BB" to an innovator product. In either case, the patient will naturally assume that the product in question must be identical to the innovator product. Further, it is impossible in the brief space available on an immediate container or product carton label to provide all information necessary to give context to this claim. Thus, inclusion of such a statement on a label is apt to mislead pharmacists and patients into concluding that the generic product is identical to the reference branded innovator product, whereas in fact, it is – at best -- merely rated "therapeutically equivalent." What could well be lost on the patient or pharmacist is the possibility of differences of the kind noted in the Guidance – *e.g.*, in scoring configuration, release mechanisms, excipients and expiration dates – that potentially could be medically significant.

Orange Book Therapeutic Equivalence Ratings Completely Meet the Need for Information

Unlike the brief statements proposed by the Guidance, the therapeutic equivalence information currently available in the *Orange Book* does not create confusion as to the source and identity of any marketed drug, and it is explained sufficiently well and updated sufficiently regularly to be of practical value. The solution to any unmet information needs of interested pharmacists and consumers would be to refer them – if need be *via* an appropriate reference in product labeling -- to the *Orange Book* listings and explanations, as available in hard copy or electronically at www.fda.gov/cder/ob/.

As the Guidance explains, the current system for providing drug information is robust:

> Drug information, as presented by the *Orange Book*, is dynamic and complex and is subject to changing conditions. As explained in the preface to the *Orange Book*, when a change occurs in the information contained in FDA files concerning a multiple-source product that is in the *Orange Book*, the potential exists that the drug product will no longer meet the criteria for therapeutic equivalence as initially evaluated. In such an instance, FDA will reevaluate the drug and, if the listed evaluation is no longer accurate, the evaluation will be revised accordingly. Revisions to the *Orange Book* are shown in monthly supplements, which are mailed to all subscribers and are available on the Internet.

The *Orange Book* is a convenient, comprehensive, readily-available, current, and easy-to-use resource that cannot be adequately supplanted by short statements on a container label. To solve even partially the problems associated with the proposed label declarations would entail taking up far, far more space on immediate container and carton labels than is available. And even if – hypothetically -- space permitted, there would still be the problem of information on marketed product labeling becoming dated.

Since health professionals currently rely on a product's package insert as the source for FDA- approved information on a prescription drug, FDA could, if need be, utilize the package insert as a vehicle for raising awareness of the *Orange Book* as the source of up-to-date information on therapeutic equivalency. A statement in the package insert of a generic product directing interested parties to the *Orange Book* for reliable and current information about therapeutic equivalence would avoid the problems described above of potentially injurious mistakes, confusion, and violation of trademark law. We therefore urge FDA to re-evaluate its position and to withdraw the Guidance.

Sincerely,

Maury M. Tepper, III
Trademark Attorney

bcc: Lesley Edwards
James Thomas
David Levy
Bill Zoffer
Michelle Hardy

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